Protocol Title:	Phase 2B/3 double-blinded placebo-controlled efficacy trial of AMPHORA® gel for the prevention of acquisition of urogenital Chlamydia trachomatis infection
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On behalf of:

Evofem, Inc.

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REVISION HISTORY

Version/Date	Version name	Section	Changes implemented
Version 0.1/ 01-Mar-2017	Initial draft version	N/A	N/A
Version 0.2/ 20-Mar-2017	Version 0.2	Cover page	Updated protocol title according to the protocol update
		Section 2	Removed the incidence of Trichomonas vaginalis (Trich) infection from exploratory objectives
		Section 3	Updated the study design Removed the randomization replacement
		Section 4	Removed proportion of subjects who experience at least one Trich infection during the study and safety endpoints
		Section 5	The dropout rate is changed from 10% to 20%. The total sample size was adjusted accordingly.
		Section 8.4.3	Added the summary of surgical/gynecologic/sexual health history per protocol update
		Section 8.7.3	Removed assessment of vaginal irritation per protocol update.
Version 0.3/ 19-Jan-2018	Version 0.3	Entire Document	Revisions throughout document to reflect protocol version 3
Version 0.4/ 02-Feb-2018	Version 0.4	Sections 8 & 9	Adherence rate analyses are clarified. Condom usage statistics were presented and testing for an effect of condom use on re-infection rates by treatment group was added. A section summarizing analyses added post-protocol was included.
Version 0.5/ 23-Apr-2018	Version 0.5	Section 2.3, section 4.3 and section 8.8.4	Add Exploratory endpoints
Version 0.6/ 19-OCT-2018	Version 0.6		Updating to reflect new protocol version.
Version 1.0/ 04-DEC-2018	Version 1.0		Reflects SAP signoff

| Version 2.0/ xx-SEP-2019 | Version 2.0 | | Clarified eligibility rules for CT & GC re-infection analyses. Added re-infection rate by visit analysis. Added AE by relationship classification analysis. Added GU adverse event summary to overall AE table. Added sensitivity analysis. Addressed the handling of subjects who enrolled into the study more than once. Revised TLF shells to reflect said updates. |

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

The following abbreviations will be used within this SAP.

AE	Adverse Event/Adverse Experience
ATC	Anatomical Therapeutic Chemical
BP	Blood Pressure
BMI	Body Mass Index
CRF	Case Report Form
CI	Confidence Intervals
CT	*Chlamydia trachomatis*
CSR	Clinical Study Report
eCRF	Electronic Case Report Form
g	Gram
GC	Neisseria gonorrhoeae
GCP	Good Clinical Practice
uHCG	(urine) Human Chorionic Gonadotropin
HIPAA	Health Insurance Portability and Accountability Act
HR	Heart Rate
ICH	International Conference on Harmonisation
ITT	Intent to Treat
MedDRA®	Medical Dictionary for Regulatory Activities
N	Number (typically refers to subjects)
PP	Per Protocol
SAE	Serious Adverse Event/Serious Adverse Experience
SMC	Safety Monitoring Committee
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TOC	Test of Cure
WHO	World Health Organization

1 INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to provide detailed descriptions of the statistical methods, data derivations and data displays for study protocol EVO-003 Version 6.0 "Phase 2B/3 double-blinded placebo-controlled efficacy trial of AMPHORA® gel for the prevention of acquisition of urogenital Chlamydia trachomatis infection" dated 25JAN2019 for CSR analysis. The table of contents and templates for the TFLs will be produced in a separate document.

Any deviations from this SAP will be described and justified in the Clinical Study Report (CSR).

The preparation of this SAP has been based on International Conference on Harmonisation (ICH) E9.

All data analyses and generation of TFLs will be performed using SAS version 9.4 or higher on the SAS Grid.

2 STUDY OBJECTIVES

2.1 Primary objective

To determine if intravaginal AMPHORA gel reduces the risk of urogenital *Chlamydia trachomatis* (CT) infection.

2.2 Secondary objective

To determine if intravaginal AMPHORA gel reduces the risk of urogenital *Neisseria gonorrhoeae* (GC) infection.

2.3 Exploratory objective

To determine if AMPHORA gel use rate (subject adherence to instructed use) has an effect on proportion of subjects who experience at least one CT or GC infection during the study intervention period.

To assess subject satisfaction (including sexual satisfaction) with AMPHORA gel over the course of the clinical trial.

3 STUDY DESIGN

3.1 General study design

Eight hundred forty-four (844) women, ages 18-45, who have had a documented urogenital infection at any time over 16 weeks (up to 118 days) preceding the enrollment visit, or found to be positive at screening visit will be enrolled. Subjects will be tested for current GC/CT infection by NAAT (vaginal swab).

A baseline vaginal pH and a full gynecologic exam (speculum) will be obtained at enrollment. Those who test positive for CT/GC infection at screening will receive standard of care (SOC) treatment. To meet eligibility criteria, these subjects will not be enrolled until 3-4 weeks after screening (at least 21 days after treatment).

Subjects are instructed to apply AMPHORA or placebo gel up to one hour prior to coitus for the duration of the 16-week intervention period. AMPHORA or placebo is to be reapplied in the same manner for each occurrence of sexual intercourse. Subjects will keep an electronic diary (eDiary) to document and track sexual activity and product use and condom use.

Every 4 weeks (5 visits) all subjects will return to the clinic for repeat CT/GC NAAT (vaginal swab), urine pregnancy (uHCG) testing, eDiary review, and return of used and unused study product. Applicators will be visually inspected for use and staining will be performed to confirm vaginal insertion of used (empty) applicators. At each Visit 2-4, subjects will be re-supplied with AMPHORA or placebo gel. At Visit 5, subjects will return used and unused study product and continue to use their e-diaries but will not be resupplied with AMPHORA or placebo gel.

Subjects will return for a follow-up visit four weeks after the intervention period. At this time, a repeat CT/GC NAAT (vaginal swab), pregnancy (uHCG) testing and eDiary review will be performed.

Screening and Eligibility

Subjects who consent may be screened if they have a known case of CT or GC within 16 weeks of enrollment, or suspicion of current CT or GC infection (subsequently confirmed with NAAT test at screening visit). Subjects randomized within 45 days of initial screening do not need to be re-screened.

Intervention and Follow-up Period

The Intervention Period is defined as Visit 1 through Visit 5. There is one follow-up visit (Visit 6), four weeks after the last intervention visit. These periods are outlined in the Schedule of Assessments. The protocol defined period of observation is 20 weeks.

Safety Follow-up After Protocol Defined Period of Observation

This period includes safety follow-up as required by Good Clinical Practice and standard clinical trial practice. Adverse events determined to be at least possibly related to the study product

continuing after the final study visit (Visit 6) will be followed until resolution or stable status as determined by the Investigator.

3.2   Randomization and blinding

This is a Phase 2B/3 placebo-controlled randomized trial, with 422 subjects per intervention arm; for a total of 844 subjects to be enrolled. The 844 subjects will be randomized using an Interactive Web Interactive System (IWRS), in a 1:1 fashion across the two intervention groups, IP or placebo. Simple randomization will be stratified by site and all documentation of this procedure will be saved with the IWRS vendor until the end of the study. Randomization will occur following enrollment and prior to issuance of study product to subjects.

On completion of the trial, after data entry is complete and the data is considered to be clean, the final database will be locked and the study will be fully unblinded.

3.3   Study treatments and assessments

Approximately 24 weeks: Screening, five intervention period visits (one every 4 weeks) and one post-intervention follow-up visit (4 weeks after the last intervention period visit). Following screening, enrollment and randomization, subjects will be issued a 4-week supply of study product based on the individual subject's projected usage. During the Intervention Period, subjects will return all unused product and used applicators packaged individually in plastic return bags provided, and be issued a new 4-week supply of study product based on projected usage. Subjects may be issued additional study product, as needed, should their supply be exhausted prior to the next study visit; however, excessive product usage should be brought to the attention of the Investigator and Sponsor. At Visit 5, subjects will return all unused product and used applicators.

Table 1 shows the study dosing for each intervention group.

Table 1: Investigational Product Dosing

Intervention Group	IP: AMPHORA gel*	Placebo: Universal Placebo Gel*
Group A	422 subjects, 5 g dose applied up to 1 hour prior to coitus**	N/A
Group B	N/A	422 subjects, 5 g dose applied up to 1 hour prior to coitus**

*The dosage of study product is 5 g (as described for each intervention group) in a pre-filled vaginal applicator.

**A detailed description of procedures and assessments to be conducted during this study is summarized in the Scheduled of Study Assessments in Table 2 below.

Table 2: Schedule of Study Assessments

Study Visit (V)	Screening[1]	Enrollment/ Visit 1[2]	Visit 2[2]	Visit 3[2]	Visit 4[2]	Visit 5[2]	Post-Intervention Follow-up/Visit 6
		Intervention Period; AMPHORA gel N=422, Placebo gel N=422					
Study Week	-4 – 0 (-30 – 0 days)	0	4	8	12	16	20
Study Product Dispensed		X	X	X	X		
Informed Consent/HIPAA	X						
Inclusion/Exclusion	X	X					
Concomitant Meds	X	X	X	X	X	X	X
AE Assessment		X	X	X	X	X	X
Medical/Sexual History	X	X					
Last Menstrual Period		X					
Physical Exam		X					
Targeted Physical Exam			[X]	[X]	[X]	[X]	[X]
Body Weight/Height		X					
Vital Signs		X					
Gynecologic Exam		X					
Urine HCG (females)		X	X	X	X	X	X
Vaginal pH		X					
Self-collected CT/GC NAAT	X		X	X	X	X	X
Clinician-collected CT/GC NAAT		X					
eDiary Set-up		X					
eDiary Review			X	X	X	X	X
Inspection of Returned Study Product			X	X	X	X	
Staining of Used Applicators			X	X	X	X	
Subject Satisfaction With Product						X	
Subject Sexual Satisfaction						X	
Female Sexual Function Index (FSFI)		X				X	
Sexual Function Questionnaire		X				X	

[1] Screening period may be up to 45 days. Subjects will be asked to return 7 days +/- 7 days after Screening Visit. If subjects NAAT results are positive, they will be first treated by SOC then will return 3 – 4 weeks after screening visit (at least 21 days after treatment) for Enrollment/Visit 1. If the screening period extends past 45 days, subjects will not be enrolled and will need to be re-screened.

[2] Patients must be asked to abstain from vaginal intercourse in the 24 hours preceding study visits 2 through 5.

4 STUDY ENDPOINTS

4.1 Primary efficacy endpoint

The primary efficacy endpoint is the proportion of subjects who experience at least one urogenital CT infection during the study intervention period (incident infection of CT).

4.2 Secondary efficacy endpoint

The secondary efficacy endpoint is the proportion of subjects who experience at least one urogenital GC infection during the study intervention period (incident infection of GC).

4.3 Exploratory endpoints

Exploratory endpoints will comprise:

- Adherence with AMPHORA gel usage during study (rate of product use adherence).
- Sensitivity analyses of the primary and secondary parameters will be performed for the following:
  - mITT Subjects with ≥20%, ≥40%, ≥60%, ≥80%, and 100% product use adherence.
  - Re-infection rate analysis with alternative definition of no re-infection
- Subject satisfaction
- Sexual satisfaction

5 SAMPLE SIZE AND POWER

The primary analysis is a comparison between proportion of subjects who experience at least one CT infection among the intervention groups (AMPHORA or placebo).

It is assumed that the proportion of patients experiencing at least one infection of CT during the study period (incident infection of CT) up to week 16 under placebo will be 22.5%. An incident infection of CT of 13% in the patients receiving active treatment (i.e., a treatment difference of 9.5%) is considered clinically relevant for AMPHORA versus placebo. Using a Chi-Square Test for the primary endpoint, 253 analyzable patients per treatment group (506 patients total in the ITT population) will yield approximately 80% power to detect 9.5% treatment difference with a 2-sided 5% type I error rate (SAS 9.3 PROC POWER). Assuming that 20% of the total enrolled patients will be lost to follow-up, 15% will be re-infected with GC (making them ineligible for the primary endpoint analysis), and 5% will be deemed ineligible for analysis due to antibiotic use, the total sample size planned for this study is 844 patients.

6 ANALYSIS POPULATIONS

This study will utilize three analysis populations: Intention-to-Treat (ITT), modified Intention-to-Treat (mITT), and safety.

6.1 Intention-To-Treat population (ITT)

The ITT population is defined as all randomized subjects. Analyses with this population will be performed based on the treatment randomized.

6.2 Modified Intention-To-Treat population (mITT)

The modified ITT population is defined as all randomized subjects who report use of study product (IP or UPG) and have negative GC/CT test result at enrollment. Analyses with this population will be performed based on the treatment randomized.

6.3 Safety population (Safety)

All randomized subjects who applied any amount of study product will be included in the Safety population. Analysis with this population will be performed based on the treatment actually received.

6.4 Protocol deviations/violations and exclusions from analysis sets

A cumulative list of protocol deviations will be reported in the Clinical Study Report.

7   STATISTICAL CONSIDERATIONS AND ANALYSIS

7.1   Derived Variables

The below table provides a list of derived variables for demographic and baseline characteristics.

Variables	Formula
Demographic and Baseline characteristics	
Age at informed consent (in years)	integer ((date of informed consent – date of birth + 1)/ 365.25)
Body mass index (BMI) (kg/m2)	weight (kg)/[height (m)]^2

7.2   Handling of missing data and outliers

No imputations will be performed for data that is missing or spurious. All analyses will be based on data as observed in the study with the exception of the following subjects that have been identified as attempting to enroll and/or successfully enrolling in the study multiple times:

1) 840-034-016/840-038-008/840-032-049
2) 840-095-013/840-097-001
3) 840-032-007/840-034-001
4) 840-075-001/840-038-003
5) 840-066-020/840-004-020
6) 840-032-048/840-034-017
7) 840-032-047/840-038-009
8) 840-075-002/840-034-005
9) 840-066-079/840-004-001

For these subjects, the following data handling rules will be applied:

1) If the subject was ultimately randomized only once, then their efficacy and applicable safety data will be counted and associated with the planned and actual treatment like any other subject.
2) To account for the presumed negligible impact of subjects were randomized multiple times the following will be done:
    a. Analyses will be run for the primary efficacy and overall AE summary table including all records associated with these subjects and will treat them as independent observations using their planned & actual treatment assignments for efficacy and safety, respectively.
    b. Analyses will be run for the primary efficacy and overall AE summary excluding

these subjects altogether from the analysis.

7.3   Analysis Eligible Subjects

When considering subjects for inclusion in the re-infection analyses, it becomes apparent that some are not appropriate for consideration. As an example, if a subject is treated with an antibiotic for an illness and this antibiotic also treats GC and/or CT, then it is not possible to get a true reflection as to the re-infection prevention abilities of the product under investigation. Likewise, if a subject is found to be infected with GC and needs to be treated, the ability to later detect a CT infection is compromised. As such, for subjects to be eligible for CT (or GC) re-infection analyses, we require the following:

1) Known re-infection status through the end of the treatment phase (i.e., a determination of positive or negative re-infection can be definitively made per definitions below),

2) No use of prohibited antibiotic medications, and

3) No GC (or CT) re-infection, unless it is identified at the same time as the CT (or GC) re-infection.

8 STATISTICAL METHODS

8.1 General statistical conventions

All statistical procedures will be completed using SAS version 9.4 or higher on the SAS Grid.

Unless otherwise stated, all statistical testing will be two-sided and will be performed using a significance (alpha) level of 0.05. Two-sided 95% confidence intervals (CI) will be provided when relevant.

For continuous variables, descriptive statistics will include the number of non-missing values, mean, standard deviation, median, minimum, and maximum. For categorical variables, descriptive statistics will include counts and percentages per category. All summaries will be presented by treatment group, unless otherwise specified.

Baseline values for all parameters will be the most recent value prior to administration of study product or speculum exam.

All subject data will be presented in individual subject data listings. Unless otherwise stated, unscheduled visit results will be included in date/time chronological order, within patient listings only. All listings will be sorted by investigational site, patient number, and visit. The treatment group (AMPHORA, Placebo) as well as patient's age and sex (if available) will be stated on each listing. With respect to study tables, the mITT population will be used for efficacy analyses; safety population will be used for safety analyses.

8.2 Subject disposition

Subject disposition information will be summarized by treatment group and overall. The number and percent of subjects who are randomized, who are randomized as replacement, who complete the study and who withdraw early from the study will be presented.

The primary reason for early withdrawal will also be tabulated.

The number of subjects randomized will be used as the denominator for the percentage calculation.

The number and percent of subjects in each analysis set and the mITT CT & GC analysis eligible subjects will also be tabulated.

Subject disposition will be listed.

8.3 Protocol deviations

The number of patients excluded from ITT, mITT, Safety analyses sets and reasons for exclusion will be summarized by treatment group and overall. Similarly, summaries of CT & GC analysis eligible patients within mITT will be presented with reasons for exclusion summarized by treatment group and overall.

All protocol deviations identified will be summarized by treatment group and overall.

A listing will include the inclusion/exclusion criteria violated at Screening and Enrollment Visits as well as other protocol deviations identified.

8.4 Demographics and baseline characteristics

Continuous measures (e.g., age, race, ethnicity, height, weight, BMI, vital signs, etc.) will be summarized treatment group and overall using descriptive statistics (n, mean median, standard deviation, 25th percentile, 75th percentile, min, and max). Meanwhile, categorical baseline characteristics will be summarized by treatment group and overall using frequency counts and percentages. All demographic & baseline information will also be in subject-level listings.

8.5 Medical history

A summary of medical/surgical/gynecologic/sexual health history will be presented by system organ class (SOC) and preferred term (PT) using Medical Dictionary for Regulatory Affairs® (MedDRA) Version 20.1 or higher. Medical history will be listed.

8.6 Concomitant medications

Concomitant medications will be assessed and includes any medication that would be taken during the study including all over the counter medications, vitamins and nutritional supplements.

Medications used in this study will be coded by using WHO drug dictionaries.

Concomitant medications will be summarized descriptively using frequency tables by ATC class and preferred name by treatment group. Concomitant medications will be listed.

8.7 Treatment adherence

Adherence with AMPHORA gel usage during study (rate of product use adherence) is defined using the gel applicators and e-diary data. Specifically, adherence will be determined using 2 methods. Method 1: adherence = # of times product is properly used as noted in the e-diary / # of coital events noted during the treatment phase in the e-diary. Method 2: adherence = # of times product is used as determined by Trypan Blue staining / # of coital events during the treatment phase noted in the e-diary. Summary statistics of adherence by method will be presented overall and by treatment group.

Study product adherence will be calculated as: 100x[adherence ratio calculated via Method 1 (or 2)]. The maximum percentage of doses used will be 100%.

Study drug compliance, times of product use (determined via e-diary & dye staining), and times of coital event will be summarized by treatment group by the number of subjects (n), mean, std dev, std error, median, min, and max.

Study drug compliance will be summarized in categories "≥20%", "≥40%", "≥60%", "≥80%", and "100%" using frequency tables. For the purposes of the frequency table, each compliance group will be deemed mutually exclusive (e.g., compliance rate of 41% would be in the ≥40% category only and would not be counted in the ≥20% category).

Treatment compliance data will be listed.

8.8 Efficacy analyses

This section addresses separately the analyses to be conducted on the primary, secondary and exploratory efficacy endpoints.

8.8.1 Analysis of primary efficacy endpoint

The primary objective of this trial is to demonstrate the efficacy of AMPHORA compared to placebo for the prevention of urogenital CT infection. The primary efficacy endpoint is the proportion of subjects who experience at least one urogenital CT infection during the study intervention period (incident infection of CT).

The primary statistical hypothesis being tested is that: There is no difference in the proportion of subjects with CT infections in the AMPHORA intervention group versus placebo. In statistical terms:

H0: $p_{AMPHORA} = p_{placebo}$, HA: $p_{AMPHORA} \neq p_{placebo}$

where $p_{AMPHORA}$ and $p_{placebo}$ denote the proportion of subjects with CT infections during the study in the AMPHORA and placebo groups, respectively.

Denominators for each proportion are the number of subjects in the mITT population in each intervention group's analysis eligible subset. To test for superiority over the placebo, the incidence of infection of CT will be compared against placebo based on a Chi-Square test. The estimate of difference in proportions, 95% confidence interval and p-value will be presented. A two-sided 5% type I error rate ($\alpha=0.05$) will be used. Note: for a subject to be considered re-infected with CT any positive NAAT test during the treatment phase (visits 1-5) will constitute re-infection. For a subject to be considered not re-infected, a subject with a negative NAAT at visits 1 & 5 with no positive NAATs in between is deemed not re-infected.

As a complementary analysis, tables will be created which also summarize re-infection by each scheduled visit.

CT infection information will be listed.

8.8.2 Analysis of secondary efficacy endpoint

Similar to the primary endpoint analysis, the incidence of urogenital GC infection will be described

using frequencies and percentages with the difference between treatment groups analysed using a Chi-Square test. Note: for a subject to be considered re-infected with GC any positive NAAT test during the treatment phase (visits 1-5) will constitute re-infection utilized. For a subject to be considered not re-infected, a subject with a negative NAAT at visits 1 & 5 with no positive NAATs in between is deemed not re-infected.

As a complementary analysis, tables will be created which also summarize re-infection by each scheduled visit.

GC infection information will be listed.

8.8.3 Analysis of exploratory endpoints

Exploratory endpoints include:

- Adherence with AMPHORA gel usage during study (see section 8.7 for more details).
- Sensitivity analyses of the primary and secondary endpoints will be performed for mITT population subjects with $\geq$20%, $\geq$40%, $\geq$60%, $\geq$80%, and 100% product use adherence (as determined via Method 1 & 2).
- Re-infection rate analysis with alternative definition of no re-infection
- Subject satisfaction, sexual satisfaction, Female Sexual Function Index and Sexual Function Questionnaire

The proportion of subjects who experience at least one CT infection during the study intervention period will be summarized by treatment group using the mITT populations and subject adherence rates. Treatment differences between AMPHORA and placebo will be tested by using Chi-square test (or Fisher Exact test, if necessary). A similar analysis will be conducted regarding GC infections. For the re-infection rate analysis with alternative definition of no re-infection, the primary & secondary endpoints will be analyzed as before with the exception that no re-infection will require negative NAAT results at Visits 1, 5 and at least 1 other schedule visit (i.e., Visits 2, 3, or 4). For satisfaction and sexual function questionnaires, descriptive statistics will be calculated for the AMPHORA group only. Listings will be provided with details for both treatment groups.

8.8.4 Other Analysis

Condom usage rates and their effect on urogenital CT re-infection rates will be explored. The rate of condom usage will be defined as # of coital acts where male condom usage is noted in the e-diary (over the course of the treatment phase) / total # of coital acts during the treatment phase.

To assess the usage rate of condoms during the study, a summary will be presented using descriptive statistics for subjects displayed by treatment group. Additionally, a summary of re-infection rates by treatment group and condom usage (none, low, high) will be presented. For the purposes of this display, low condom use will be defined as subjects that have a rate that is less than or equal to the 50th percentile of subjects using condoms (i.e., no condom use will not be used for the 50th percentile calculation).

8.9 Safety analyses

All safety data will be summarized by intervention group. Safety analyses will be conducted on the Safety Analyses Set and will be performed for all safety variables specified below.

No statistical tests will be performed.

8.9.1 Adverse events

A summary of all adverse events that were reported will be presented by Medical Dictionary for Regulatory Activities® (MedDRA®-version 20.1 or higher) coding (System Organ Class and Preferred Term) by highest severity (one report by highest severity for each subject for that adverse event).

The incidence of adverse events (new or worsened) will be summarized by system organ class, preferred term, severity, and relationship to study intervention. The incidence of death, SAEs, and AEs leading to discontinuation will be summarized separately by system organ class and preferred term. Lastly, a summary of AEs by system organ class and relationship to study interventions will be provided.

An overall AE table will also be provided which provides a high-level of AE findings. As a part of this summary, subject & event counts for genitourinary events of FDA interest will be noted.

All adverse events will be listed.

8.9.2 Clinical laboratory evaluations

Specimens collected for NAATs will be processed by the sites and shipped to a central laboratory for testing. All other laboratory testing and staining of used applicators will be performed on-site.

Vaginal pH, NAATs for CT/GC, staining of used applicators, and urine β-human chorionic gonadotropin (uHCG) will be summarized by visit for each treatment group. Listings will be provided as well.

8.10 Interim analysis

There are no interim analyses planned.

9 ANALYSIS CHANGES FROM THE PROTOCOL

The following changes to the analysis plan have changed since the approval of the protocol:

1) Male condom usage summary statistics.

2) Assessing the effect of male condom usage on re-infection rates.

3) The data handling rules associated with subjects who enrolled multiple times in the study.

4) CT/GC re-infection rate sensitivity analysis

5) CT/GC re-infection rate summaries by timepoint

6) GU events summary added to the overall AE summary table

7) The mITT population has been relaxed to allow any randomized subject who uses product, whether or not there is coitus, and has negative CT/GC NAATs at baseline.

10   REFERENCES

1. ICH Topic E3: Structure and Content of Clinical Study Reports (CPMP/ICH/137/95-adopted December 1995).

2. ICH Topic E9: Statistical Principles for Clinical Trials (CPMP/ICH/363/96 – adopted March 1998).

3. EVO-003 Protocol Version 6.0, 25JAN2019.